

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Previously Cancelled).

2. (Currently Amended) A nucleic acid molecule comprising at least a first signal sequence and a second signal sequence and a recombinase gene operably linked to an expression control sequence, said first and second signal sequences being positioned to mediate ~~excision or~~ inversion of a sufficient portion of either the recombinase gene or the expression control sequence to inactivate or decrease recombinase activity when the first and second signal sequences are contacted with a recombinase, thereby decreasing or eliminating recombinase-mediated toxicity.

3. (Previously Amended) The nucleic acid molecule of claim 2, wherein said nucleic acid molecule is included in a retroviral vector and said signal sequence is inserted into a retroviral long terminal repeat of said vector.

4. (Originally Presented) The nucleic acid molecule of claim 3, wherein said signal sequence is inserted into the U3 region of the 3' retroviral long terminal repeat of said vector.

5. (Previously Amended) The nucleic acid molecule of claim 2, wherein said recombinase is selected from the group consisting of a *cre* recombinase and a Flp recombinase and the signal sequence is selected from the group consisting of lox sequences and FRT sequences.

6. (Previously Cancelled).

7. (Previously Amended) The nucleic acid molecule of claim 2, wherein said signal sequences flank said recombinase gene or said expression control sequence of said recombinase gene.

8. (Previously Amended) A cell comprising the nucleic acid molecule of claim 2.

9. (Originally Presented) The cell of claim 8, further comprising a second nucleic acid molecule comprising a target gene and signal sequences recognized by said recombinase.

*isolated*

8. (Currently Amended) The cell of claim 9, wherein said recombinase, when expressed in said cell, excises or inverts a sequence in said second nucleic acid molecule that is located between said signal sequences in said second nucleic acid molecule, and the excision or inversion results in modulation of expression of said target gene, thereby decreasing or eliminating recombinase-mediated toxicity.

*isolated*

9. (Currently Amended) The cell of claim 10, wherein said signal sequences in said second nucleic acid molecule are in inverted direct orientation with respect to one another.

*isolated*

10. (Currently Amended) The cell of claim 11, wherein said signal sequences in said second nucleic acid molecule flank said target gene, so that expression of said recombinase results in inversion excision of said target gene, and inactivation of expression of said target gene.

*isolated*

11. (Currently Amended) The cell of claim 12, wherein said signal sequences in said second nucleic acid molecule flank a positive regulatory element of said target gene, so that expression of said recombinase results in inversion excision of said positive regulatory element, and inactivation of expression of said target gene.

*An isolated*

12. (Allowed) A cell comprising two nucleic acid molecules, wherein the first nucleic acid molecule comprises a recombinase gene operably linked to an expression control sequence and signal sequences recognized by a recombinase and the second nucleic acid molecule comprises a target gene and signal sequences recognized by a recombinase, wherein said signal sequences in said second nucleic acid molecule flank a negative regulatory element of said target gene, so that expression of said recombinase results in excision of said negative regulatory element, and activation of expression of said target gene.

*An isolated*

13. (Allowed) A cell comprising two nucleic acid molecules, wherein the first nucleic acid molecule comprises a recombinase gene operably linked to an expression control sequence and signal sequences recognized by a recombinase and the second nucleic acid molecule comprises a target gene and signal sequences recognized by a recombinase, wherein said signal sequences in said second nucleic acid molecule are in an inverted orientation with respect to one another.

*isolated*

14. (Allowed) The cell of claim 13, wherein said signal sequences in said second nucleic acid molecule flank an inverted positive regulatory element of said target gene or an inverted coding

region of said target gene, so that expression of said recombinase results in inversion of said inverted positive regulatory element or inversion of said inverted coding region, and activation of expression of said target gene.

15. (Allowed) The cell of claim <sup>13</sup>~~15~~, wherein said signal sequences in said second nucleic acid molecule flank an inverted negative regulatory element of said target gene or a coding region of said target gene, so that expression of said recombinase results in inversion of said inverted negative regulatory element or inversion of said coding region, and inactivation of expression of said target gene.

16. (Originally Presented) The cell of claim <sup>8</sup>~~13~~, wherein said signal sequences in said nucleic acid molecule comprising said sequence encoding said recombinase flank said nucleic acid sequence encoding said recombinase.

17. (Originally Presented) The cell of claim <sup>8</sup>~~13~~, wherein said signal sequences in said nucleic acid molecule comprising said sequence encoding said recombinase flank a positive regulatory element of said nucleic acid sequence encoding recombinase.

18. (Originally Presented) The cell of claim <sup>9</sup>~~8~~, wherein said nucleic acid molecule comprising said sequence encoding said recombinase and said second nucleic molecule are present in the same vector.

19. (Allowed) A cell comprising two nucleic acid molecules, wherein the first nucleic acid molecule, comprising a recombinase gene operably linked to an expression control sequence and signal sequences recognized by a recombinase and the second nucleic acid molecule, comprising a target gene and signal sequences recognized by a recombinase, are present in separate vectors.

22-50. (Cancelled).

20. (New) The nucleic acid molecule of claim <sup>1</sup>~~2~~, wherein said signal sequences are in inverted orientation with respect to one another.